

The Effects of Biphasic and Conventional Monophasic Defibrillation on Postresuscitation Myocardial Function

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- OBJECTIVES** The purpose of this study was to compare the effects of biphasic defibrillation waveforms and conventional monophasic defibrillation waveforms on the success of initial defibrillation, postresuscitation myocardial function and duration of survival after prolonged ventricular fibrillation (VF).
- BACKGROUND** We have recently demonstrated that the severity of postresuscitation myocardial dysfunction was closely related to the magnitude of the electrical energy of the delivered defibrillation shock. In the present study, the effects of fixed 150-J low-energy biphasic waveform shocks were compared with conventional monophasic waveform shocks after prolonged VF.
- METHODS** Twenty anesthetized, mechanically ventilated domestic pigs were investigated. VF was induced with an AC current delivered to the right ventricular endocardium. After either 4 or 7 min of untreated ventricular fibrillation (VF), the animals were randomized for attempted defibrillation with up to three 150-J biphasic waveform shocks or conventional sequence of 200-, 300- or 360-J monophasic waveform shocks. If VF was not reversed, a 1-min interval of precordial compression preceded a second sequence of up to three shocks. The protocol was repeated until spontaneous circulation was restored or for a total of 15 min.
- RESULTS** Monophasic waveform defibrillation after 4 or 7 min of untreated VF resuscitated eight of 10 pigs. All 10 pigs treated with biphasic waveform defibrillation were successfully resuscitated. Transesophageal echo-Doppler, arterial pressure and heart rate measurements demonstrated significantly less impairment of cardiovascular function after biphasic defibrillation.
- CONCLUSIONS** Lower-energy biphasic waveform shocks were as effective as conventional higher energy monophasic waveform shocks for restoration of spontaneous circulation after 4 and 7 min of untreated VF. Significantly better postresuscitation myocardial function was observed after biphasic waveform defibrillation. (J Am Coll Cardiol 1999;34:815-22) © 1999 by the American College of Cardiology

Both clinical and experimental studies have demonstrated substantial impairment of ventricular function after resuscitation from cardiac arrest (1-5). Indeed, postresuscitation myocardial dysfunction has been implicated as a potentially important mechanism accounting for fatal outcomes after successful resuscitation in 70% of victims within the first 72 h (1,2). Recent studies from our institute on a murine model implicated the total electrical energy delivered during defibrillation as an important correlate with the severity of postresuscitation myocardial dysfunction and postresuscita-

tion survival (6). This prompted us to investigate the option of utilizing lower electrical energy biphasic waveform defibrillation.

Currently available external defibrillators utilize two waveform morphologies. Biphasic waveforms deliver both a positive and a negative current with evidence of successful defibrillation utilizing significantly lower energy levels. Lower biphasic waveform defibrillation energy requirements have been demonstrated with short-duration ventricular fibrillation (VF) in both animal and human electrophysiologic laboratories (7-10). Recent observations with 150-J biphasic waveform shocks on out-of-hospital cardiac arrest victims also indicate the potential benefits of lower defibrillation energies (11,12).

Monophasic waveforms represent damped sinusoidal waveforms or truncated exponential waveforms. In settings of cardiac arrest, monophasic waveforms are currently the most common waveforms utilized for transthoracic defibril-

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Abbreviations and Acronyms

CPR	= cardiopulmonary resuscitation
EF	= ejection fraction
FAC	= fractional area change
FiO ₂	= fractional inspired oxygen
LVEDV	= left ventricular end-diastolic volume
LVESV	= left ventricular end-systolic volume
LVWD	= diastolic left ventricular posterior wall thickness
LVWS	= systolic left ventricular posterior wall thickness
P _{ET} CO ₂	= end-tidal PCO ₂
SV	= stroke volume
VF	= ventricular fibrillation

lation, both with manual and with automatic external defibrillators. The American Heart Association Guidelines advise an initial 200-J shock with increases in energy levels to either 200 or 300 J and then to 360 J for subsequent shocks (13).

In the present study, low-energy biphasic waveform defibrillation and conventional monophasic waveform defibrillation were related to the success of initial defibrillation, postresuscitation myocardial function and duration of survival after either 4 or 7 min of untreated cardiac arrest. We hypothesized that biphasic waveform defibrillation with a fixed energy of 150 J may be as effective as conventional monophasic damped sine waveform defibrillation with increasing energies ranging from 200 to 360 J after prolonged cardiac arrest. We further anticipated lesser severity of postresuscitation myocardial dysfunction with the 150-J biphasic waveform defibrillation.

METHODS

The protocol was approved by the Institutional Animal Care and Use Committee. All animals received humane care in compliance with the *Principles of Laboratory Animal Care* formulated by the National Society for Medical Research and the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH publication 86-32, revised 1985).

Animal preparation. Male domestic pigs weighing between 40 and 45 kg were fasted overnight except for free access to water. Anesthesia was initiated by intramuscular injection of ketamine (20 mg/kg) and completed by ear vein injection of sodium pentobarbital (30 mg/kg). Additional doses of sodium pentobarbital (8 mg/kg) were injected to maintain anesthesia at intervals of 1 h. A cuffed endotracheal tube was advanced into the trachea. Animals were mechanically ventilated with a volume controlled ventilator (Model MA-1; Puritan-Bennett, Carlsbad, California). End-tidal PCO₂ (P_{ET}CO₂) was monitored with an infrared analyzer (Model 01R-7101A; Nihon Kohden Corp, Tokyo,

Japan). Respiratory frequency was adjusted to maintain P_{ET}CO₂ between 35 and 40 mm Hg.

For the measurement of left ventricular function, a 5-MHz single plane with 5-MHz continuous-wave Doppler transesophageal echocardiographic transducer with four-way flexure (Model 21363A; Hewlett-Packard Co., Medical Products Group, Andover, Massachusetts) was advanced from the incisor teeth into the esophagus for a distance of approximately 35 cm. For the measurement of aortic pressure, a fluid-filled catheter was advanced from the left femoral artery into the thoracic aorta. For the measurements of right atrial pressure, pulmonary arterial pressures and blood temperature, a 7-F, pentalumens, thermodilation-tip catheter was advanced from the left femoral vein and flow directed into the pulmonary artery. For inducing VF, a 5-F pacing catheter (EP Technologies, Inc., Mountain View, California) was advanced from the right cephalic vein into the right ventricle until an electrocardiographic current of injury was recorded.

Experimental procedures. Five minutes before inducing cardiac arrest, the animals were randomized to either biphasic defibrillation or monophasic defibrillation by the sealed envelope method. The VF was induced by progressively increasing an AC current to the endocardium of the right ventricle from 1 to 2 mA. Mechanical ventilation was discontinued after onset of VF. After either 4 or 7 min of untreated VF, defibrillation was attempted with either a defibrillator designed to manually deliver up to three biphasic waveform shocks with a nominal energy level of 150 J (Forerunner AED; Heartstream, Seattle, Washington) or by a conventional monophasic waveform defibrillator, which provided energy levels of up to 360 J (Codemaster XL defibrillator; Hewlett-Packard). The shocks were delivered between a (positive) right infraclavicular electrode and a (negative) cardiac apical electrode. If VF was not reversed after three shocks or a pulseless rhythm was encountered after shock(s), precordial compression was begun utilizing a pneumatic piston-driven chest compressor (Thumper, Model 1000; Michigan Instruments, Grand Rapids, Michigan). At the start of precordial compression, the animals were mechanically ventilated with tidal volume of 15 ml/kg and FiO₂ (fractional inspired oxygen) of 1.0. Precordial compression was programmed to provide 80 compressions per minute and synchronized to provide a compression/ventilation ratio of 5:1 with equal compression-relaxation intervals, (i.e., a 50% duty cycle). The compression force was adjusted to decrease the anterior-to-posterior diameter of the chest by 25%, such as to maintain the coronary perfusion pressure within the range of 15 ± 2 mm Hg. After each minute of precordial compression, another sequence of up to three shocks (150 J for each biphasic defibrillation and 200, 300, and 360 J for monophasic defibrillation) were delivered. Defibrillation was repeated at intervals of 1 min until the animal was successfully resuscitated or for a maximum of 15 min. No vasopressor and, more specifically, no epineph-

Table 1. Outcomes after Biphasic and Monophasic Defibrillation

Group	Duration of VF (min)	Transthoracic Impedance (ohms)	Defibrillation Energy (J)	Duration of CPR (min)	ROSC	72-hour Survival
Monophasic	4	54.0 ± 5.1	684 ± 546	4.2 ± 6.0	4/5	4/5
Biphasic	4	54.6 ± 12.3	300 ± 0	0.8 ± 0.8	5/5	5/5
Monophasic	7	48.4 ± 3.9	2,276 ± 1,113*	5.4 ± 5.3	4/5	3/5
Biphasic	7	60.2 ± 3.9	450 ± 300	1.6 ± 0.5	5/5	5/5

*p < 0.01 vs. biphasic.

Data are mean ± SD. CPR = cardiopulmonary resuscitation; ROSC = restoration of spontaneous circulation; VF = ventricular fibrillation.

rine was administered during cardiopulmonary resuscitation (CPR) to avoid the additional variables including the detrimental beta-adrenergic effects of epinephrine on postresuscitation myocardial function (3). If an organized cardiac rhythm with mean aortic pressure of more than 60 mm Hg persisted for an interval of 5 min or more, the animal was regarded as successfully resuscitated. Animals were then monitored for an additional 4 h. After the panel of 4-h postresuscitation measurements had been completed, the animals were returned to their cages and observed for an additional 68 h. At the end of the 72-h postresuscitation interval, echo-Doppler measurements of myocardial function were repeated. The animals were then killed by intravenous injection of 150 mg/kg pentobarbital. Autopsy was routinely performed such as to identify any significant injuries to the bony thorax or the thoracic and abdominal viscera during CPR, which would have precluded inclusion of the animal in the study.

Measurements. Dynamic data, including aortic, right atrial, pulmonary artery and pulmonary occlusive pressures, $P_{ET}CO_2$ and the lead two electrocardiograms together with the digital output of the Acoustic Quantification system (Hewlett-Packard Co.) were continuously measured and recorded on a PC-based data acquisition system, supported by CODAS hardware/software as previously described (14-16). A total of 16 channels were provided for continuous recording at appropriate sampling frequencies. The coronary perfusion pressure was digitally computed from the differences in time-coincident aortic and right atrial pressures and displayed in real time. The transthoracic electrical impedance was recorded for each shock.

Myocardial systolic and diastolic functions were measured with transesophageal echo-Doppler techniques developed by us for this porcine model (17). Echocardiographic measurements were obtained with the aid of the echocardiographic system (Sonos 2500; Hewlett-Packard Co.). A long-axis four-chamber view or, alternatively, a technically satisfactory two-chamber view was obtained in each experiment. Left ventricular end-systolic and -diastolic volumes were calculated by the method of discs utilizing acoustic quantification technology (Hewlett-Packard Co.). Ejection fraction, stroke volume and the rate of change of ventricular volumes were computed. Cardiac output was calculated as the product of transaortic flow time velocity integral, aortic

valve diameter and heart rate. Measurements of left ventricular end-diastolic volumes and wall thickness served as indicators of diastolic function.

A quantitative neurological alertness score developed by our group (16) was utilized for evaluating neurologic recovery at 12-h intervals for a total of 72 h. The alertness score was based on objective grading of level of consciousness, respiration, posture and food and water intake. Alertness was scored from 0 (coma) to 100 (fully alert).

Aortic and mixed venous blood gases, hemoglobin and oxyhemoglobin were measured with an automated blood gas analyzer and a Co-Oximeter (Models 1306 and 482; Instrumentation Laboratory, Lexington, Massachusetts) adapted for porcine blood. Arterial blood lactate was measured with a lactic acid analyzer (model 23L; Yellow Springs Instruments, Yellow Springs, Ohio). These measurements were obtained 30 min before cardiac arrest and at hourly intervals after resuscitation for a total of 4 h.

Analysis. For measurement between groups, analysis of variance (ANOVA) and Scheffe's multicomparison techniques were used. Comparisons between time-based measurements within each group were performed with ANOVA repeated measurements. When the dependent variable was categorical, including success of resuscitation and 24-, 48- and 72-h survival, Fisher exact test was used.

RESULTS

A total of 21 experiments were performed and completed. One animal demonstrated massive bleeding into the thorax at autopsy caused by laceration of the left lung by fractured ribs. This experiment was excluded. There were no differences in hemoglobin and oxyhemoglobin, blood gas measurements, arterial lactate, $P_{ET}CO_2$, pulmonary artery pressure, right atrium pressure, the calculated coronary perfusion pressure and neurologic alertness score among the four groups before cardiac arrest and after successful resuscitation. No significant differences in transthoracic impedance were demonstrated among the groups after either 4 or 7 min of untreated VF (Table 1). No differences in the efficacy of defibrillation were demonstrated among the groups. Both biphasic and monophasic defibrillation con-

4 MINUTES VF

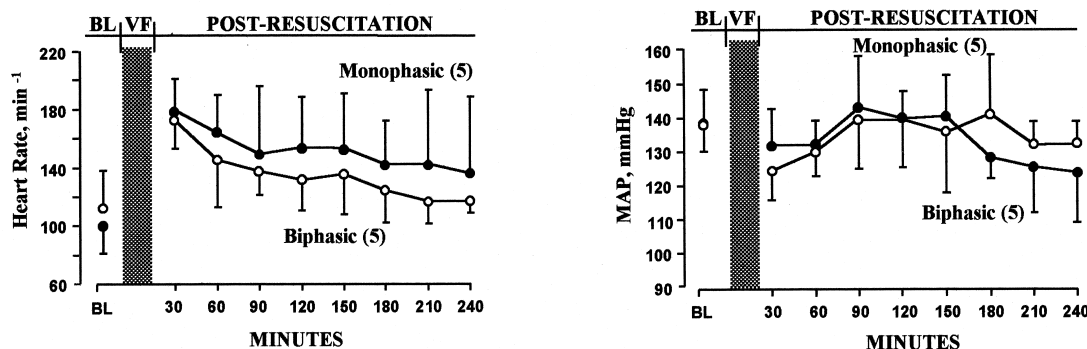


Figure 1. Effects of biphasic or monophasic defibrillation waveform on heart rate and mean aortic pressure (MAP) after either 4 or 7 min of untreated VF. Values are mean \pm SD. BL = baseline. * $p < 0.05$ vs. biphasic, ** $p < 0.01$ vs. biphasic.

verted VF to spontaneous circulation or electromechanical dissociation after the first shock in three of five animals in each group, both after 4 and after 7 min of untreated VF.

All 10 animals treated with biphasic waveform defibrillation were successfully resuscitated after either 4 or 7 min of untreated VF. Monophasic waveform defibrillation after 4 min of untreated VF allowed four of five animals to be successfully resuscitated. Monophasic waveform defibrillation after 7 min of untreated VF also yielded four of five successful resuscitations (Table 1). Numerically greater defibrillation energies were utilized in animals after monophasic defibrillation in which there was a greater incidence of recurrent VF before restoration of spontaneous circulation. However, the increases in delivered energies were statistically different only in the groups of animals after 7 min of untreated VF (Table 1). After monophasic waveform defibrillation, animals required numerically more prolonged precordial compression. However, large variances were encountered such that the differences were not statistically significant (Table 1).

When successful defibrillation followed 4 min of untreated VF, no differences in mean aortic pressure were observed between biphasic and monophasic groups after successful resuscitation. However, when successful defibrillation followed 7 min of untreated VF, a significantly lower mean aortic pressure and significantly greater heart rate were observed after monophasic defibrillation (Fig. 1).

Myocardial function was reduced in all animals after successful resuscitation. However, significantly less impairment followed biphasic defibrillation (Fig. 2). After 4 min of untreated VF, left ventricular stroke volume (SV), ejection fraction (EF), fractional area change (FAC) and left ventricular end-diastolic volume (LVEDV) were each significantly greater after biphasic defibrillation.

When the duration of untreated VF was increased from 4 to 7 min, these differences in postresuscitation myocardial function were magnified (Fig. 3). After biphasic waveform defibrillation, left ventricular FAC indicated better contractile function in association with greater EF, SV, and cardiac output. The differences in left ventricular end-systolic volume (LVESV) and LVEDV indicated that

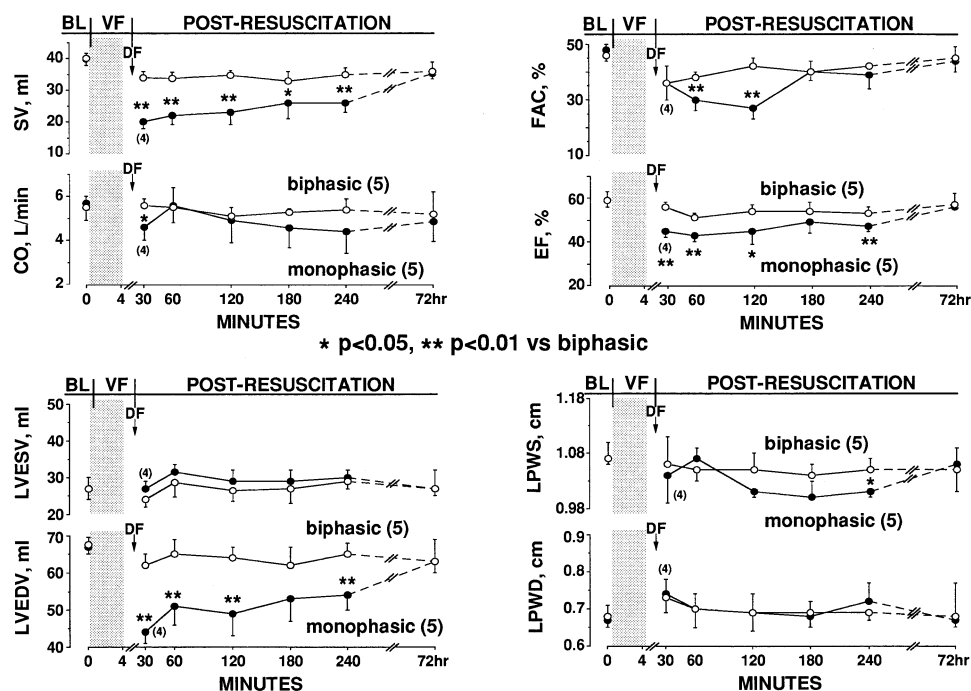


Figure 2. Effects of biphasic or monophasic defibrillation waveform on postresuscitation myocardial function after 4 min of untreated VF. Values are mean \pm SD. BL = baseline, CO = cardiac output, SV = stroke volume, LPWS = systolic left ventricular posterior wall thickness, LPWD = diastolic left ventricular posterior wall thickness. * $p < 0.05$ vs. biphasic, ** $p < 0.01$ vs. biphasic.

biphasic waveform defibrillation yielded less impairment of left ventricular function. Because both systolic and diastolic left ventricular posterior wall thickness (LVWS and LVWD) were significantly less after biphasic defibrillation,

there was evidence of better myocardial compliance after biphasic defibrillation (Fig. 3).

All animals survived for more than 72 h after biphasic waveform defibrillation, both after 4 or 7 min of untreated

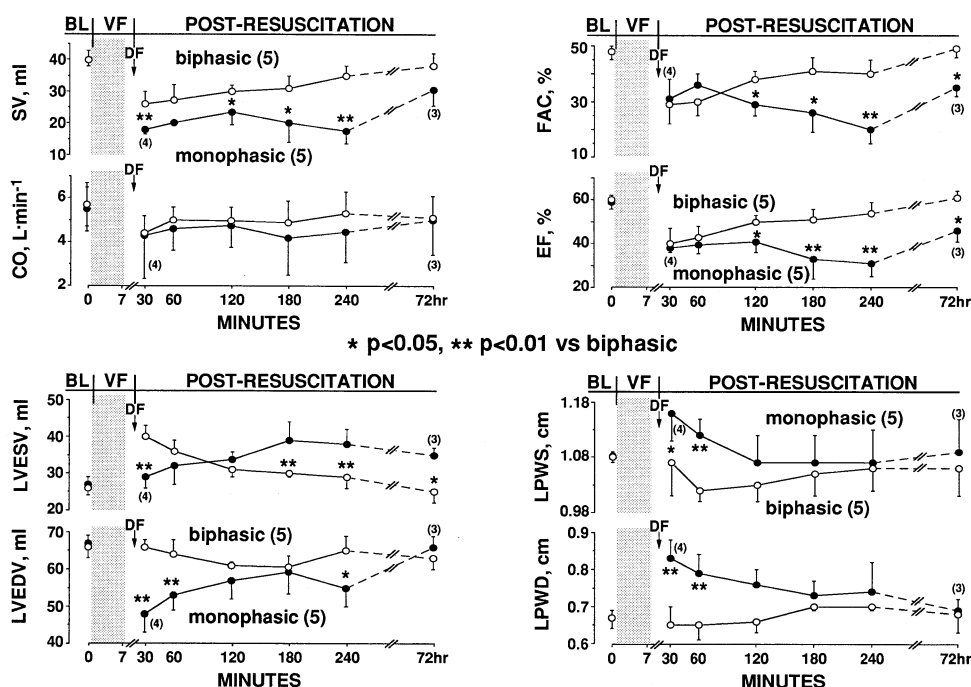


Figure 3. Effects of biphasic or monophasic defibrillation waveform on postresuscitation myocardial function after 7 min of untreated VF. Values are mean \pm SD. BL = baseline, CO = cardiac output, SV = stroke volume, LPWS = systolic left ventricular posterior wall thickness, LPWD = diastolic left ventricular posterior wall thickness. * $p < 0.05$ vs. biphasic, ** $p < 0.01$ vs. biphasic.

VF. With monophasic defibrillation after 4 min of untreated VF, four of five animals survived for more than 72 h. After 7 min of untreated VF with monophasic defibrillation, three of five animals survived for more than 72 h. However, these differences, were not statistically significant (Table 1).

DISCUSSION

The present study demonstrated that biphasic waveform defibrillation with lower delivered energies was as effective or potentially more effective than monophasic waveform with respect to success of resuscitation, postresuscitation myocardial function and 72-h survival after up to 7 min of untreated VF. Myocardial contractility as measured by left ventricular stroke volume, EF, FAC, LVESV and LVEDV was significantly greater in animals with biphasic defibrillation after 4 min of untreated VF. When the duration of untreated VF was prolonged to 7 min, the impairment of myocardial contractility was magnified in animals with monophasic defibrillation together with impaired myocardial compliance as evidenced by increased left ventricular wall thickness. Because the duration of untreated VF and the coronary perfusion pressure produced by chest compression were controlled in the present study, the differences in postresuscitation myocardial function are likely to reflect difference in either the waveforms or in the total energy delivered. Moreover, biphasic waveform, which provided shocks with smaller energy level, was at least as effective for successful resuscitation and produced significant lesser impairment in postresuscitation myocardial function.

Clinical implications. Postresuscitation myocardial dysfunction significantly compromises outcomes of CPR. Although the initial success of CPR from sudden death is approximately 39% (range 13% to 59%), most victims die within 72 h after initially successful resuscitation, primarily due to ventricular arrhythmias and heart failure. The CPR itself therefore provides ultimate survival for as few as 3% to 5% of victims (1,2,18,19). The severity of postresuscitation myocardial dysfunction was previously related to the duration of cardiac arrest, to treatment with epinephrine and to hypercarbic myocardial acidosis (3,4). The predecessor study (6) and the present study have implicated the total electrical energy delivered during defibrillation attempts as an additional factor. We are therefore prompted to call attention to the potential importance of minimizing the electrical energy delivered during electrical defibrillation attempts such as to preserve maximal postresuscitation myocardial function and thereby improve survival.

Defibrillation-induced myocardial injury. After direct current transthoracic defibrillation was introduced for the treatment of VF by Lown et al. (20), both the magnitude and duration of the transthoracic electrical shock utilized for defibrillation from VF were suspect as causes of myocardial injury. However, in studies performed on intact animals under physiologic conditions, such was not the case. In their

famed *Textbook of Physiology*, Guyton and Hall (21) referred to earlier experiences with electrical defibrillation. They regarded it as a benign insult. Guyton and Hall delivered 130 transthoracic shocks to one normal, anesthetized dog and noted no adverse effects on the circulation. Kerber et al. (22) utilized repetitive transthoracic shocks with delivered energy of 460 J without adverse effects on the heart rate, arterial pressure or left ventricular end-diastolic pressure in normal dogs. Recently, Kern et al. (21) found that five transthoracic shocks with a cumulative total of 886 J did not adversely affect left ventricular ejection fraction in anesthetized pigs with spontaneous circulation. Multiple high-power electrical shocks, delivered under physiologic conditions in hemodynamically stable animals, may not impair the function of the heart.

However, such a benign observation does not necessarily apply to the ischemic heart. In isolated tissue cultures of myocardial cells, irregularities of contraction followed a single shock with a peak intensity of either 80 or 200 V/cm (24). Synchronized shocks with an energy of 35 J applied directly to the fibrillating canine ventricle significantly decreased cardiac output (25). After cardiac arrest in dogs, a transthoracic 400-J countershock produced both histologic and metabolic impairment of myocardial cells (26). After successful defibrillation of patients who sustained cardiac arrest, postresuscitation hypotension and decreased postresuscitation survival were documented (27,28).

Biphasic defibrillation waveform reduces the energy of defibrillation. During the past two decades, biphasic waveform defibrillation has been examined in experimental and clinical settings of VF. Biphasic waveforms achieved successful defibrillation with significantly lower delivered energy comparable with that of monophasic waveforms when VF was of short duration (<60 s) (7-10). In the design of automatic implantable cardioverter-defibrillators, the advantages of low-energy intracardiac and transvenous biphasic defibrillation were widely recognized (29-33). By the early 1990s, all implantable defibrillators were designed to utilize biphasic waveforms.

In the human electrophysiology laboratory or operating room, impedance-compensating biphasic waveforms with energy levels of 115 or 130 J were as effective as monophasic waveforms with higher energy levels of 200 or 360 J for up to 15 s after VF had been induced (9,10). After prolonged VF in out-of-hospital settings, there was evidence of a greater number of successful defibrillation rates with 150-J impedance-compensating biphasic waveform when compared with monophasic waveform (11,12). The present study demonstrated that after prolonged VF, the biphasic waveform defibrillation improved the numerical success of initial resuscitation in that each of 10 animals was resuscitated with biphasic waveform defibrillation, but only seven of 10 with monophasic waveform defibrillation. Yet, these differences were not statistically significant. However, statistically significant improvement in postresuscitation myo-

cardiac and hemodynamic function followed successful resuscitation with lower energy biphasic waveform shocks.

Potential mechanisms. Although the differences between outcomes with monophasic and biphasic waveforms are highly significant, understanding of the myocardial injury caused by the electrical shock is as yet incomplete. In the present study, we compared electrical shocks in which there were differences both in the waveforms and the total energy delivered. Accordingly, the results leave unanswered whether the differences in postresuscitation myocardial function are related to the waveforms, the total energies or a combination of the two. Indeed, a more precise understanding of mechanisms is the subject of continuing research by our group (34). Histologic assessment has not as yet proved fruitful. Increases in free ascorbyl radicals in coronary sinus blood after defibrillation were directly proportional to the delivered energy (35). These free radicals may explain impaired organellar function with damaged sarcolemma and mitochondria, calcium overload and impaired cellular oxidative metabolism (36). The role of adrenergic receptor functions and especially beta-adrenergic receptors is also being explored (3).

Conclusions. The experimental data herein reported sustains each of our hypotheses. Biphasic waveform shocks with a fixed energy of 150 J were as effective as conventional sequential monophasic waveform with progressive energy levels of 200, 300 and 360 J for successful defibrillation. However, the low-energy biphasic waveform shocks significantly decreased the severity of postresuscitation myocardial dysfunction.

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